REMARKS

Claims 1-11 and 30-34 are currently pending. No claims have been amended herein. Applicants respectfully request reconsideration and allowance of all pending claims.

1. Rejection of the Claims under 35 U.S.C. §103(a) over Phinney, et al., Visser, et al., and Bren

Reconsideration is requested of the rejection of claims 1-4, 6, and 30-33 under 35 U.S.C. §103(a) as being unpatentable over Phinney, et al. (WO 03/043570) in view of Visser, et al. ("Elevated C-Reactive Protein Levels in Overweight and Obese Adults", Journal of the American Medical Association, 1999; 282:2131-215) and Bren ("Losing Weight: Start by Counting Calories," FDA Consumer Magazine, Jan-Feb 2002, Pub. No. FDA 04-1303C, p. 1-6).

Initially, applicants note that the rejections over Phinney, et al., Visser, et al., and Bren are substantially the same as those set forth in the previous Office action dated October 15, 2009. Consequently, many of the Office's comments have previously been addressed in applicants' response of January 19, 2010. For the sake of brevity, applicants do not now repeat those comments in full, but rather incorporate herein by reference the comments made in the January 19, 2010 response.

Claim 1 is directed to a method for decreasing the appetite of an obese or overweight mammal comprising enterally administering at a time prior to or in conjunction with an appetite-impacting stimulus to said mammal an amount of long-chain n-3 polyunsaturated fatty acid effective to decrease the

appetite of said mammal, wherein the polyunsaturated fatty acid has 20 or more carbon atoms, and wherein the polyunsaturated fatty acid is administered in the form of a triacylglycerol to treat obesity or overweight in mammals that are obese or overweight, and wherein the appetite of the mammal needs to be decreased, and the long-chain n-3 polyunsaturated fatty acid is administered to the mammal for the purpose of decreasing the appetite of the mammal.

Phinney, et al. disclose formulations and methods for the treatment and/or amelioration of symptoms of inflammatory conditions and associated systemic inflammatory responses. Phinney, et al. disclose that elevated levels of C-reactive protein (CRP) have been associated with some of these various inflammatory conditions. The formulations comprise a non-alpha tocopherol (especially gamma-, beta-, or delta-tocopherol) and one or more of an omega-3 fatty acid, such as docosahexaenoic acid (DHA) or a flavonoid.

Significantly, Phinney, et al. fail to disclose a method of enterally administering at a time prior to or in conjunction with an appetite-impacting stimulus to an obese or overweight mammal an amount of long-chain n-3 polyunsaturated fatty acid effective to decrease the appetite of said mammal, wherein the appetite of said mammal needs to be decreased. More particularly, nowhere is there any mention of an appetite-impacting stimulus in the Phinney, et al. reference. Phinney, et al. furthermore fail to disclose administering an amount of long-chain n-3 polyunsaturated fatty acid effective to decrease

the appetite of said mammal for the purpose of decreasing the appetite of the mammal.

Recognizing that the Phinney, et al. reference fails to teach or suggest each and every limitation of Applicants' claimed invention, the Office cites the Visser, et al. and Bren references for combination with Phinney, et al.

Visser, et al. describes a study that used the guideline parameter of body mass index to identify patients that are overweight or obese and have the C-reactive protein biomarker. Visser, et al. found that both overweight and obese persons were more likely to have elevated CRP levels than their normal-weight counterparts.

Bren generally describes issues arising due to obesity or overweight. Bren indicates that in order to lose weight, one can eat a low calorie, low-fat diet, limit portion size, and increase physical activity.

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. §2142 requires a clear articulation of the reasons why the claimed invention would have been obvious. Specifically, the Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 82 USPQ2d 1385, 1396 (2007) noted that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some **articulated reasoning** with some **rational underpinning** to support the legal conclusion of obviousness." The Court in KSR International

further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art references that would have led one of ordinary skill to modify/combine the prior art references to arrive at the claimed invention.

Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding that there was reasonable expectation of success; and (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as the combined reference teachings fail to teach or suggest each and every limitation of claim 1, and further, there is no apparent reason for one skilled in the art to modify or combine the reference teachings to arrive at each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed combinations.

For the reasons set forth in the response of January 19, 2010, applicants submit there is no apparent reason to modify or combine the cited references to arrive at the claimed limitation of enterally administering at the time prior to or in conjunction with an appetite-impacting stimulus to an obese or overweight mammal an amount of long-chain n-3 polyunsaturated fatty acid effective to decrease the appetite of said mammal, wherein the long-chain n-3 polyunsaturated fatty acid is administered to the mammal for the purpose of decreasing the appetite of the mammal. Nor is there any apparent reason to modify or combine the cited references to arrive at a method for decreasing the appetite of an obese or overweight mammal by enterally administering to the obese or overweight mammal an amount of long-chain n-3 polyunsaturated fatty acid effective to decrease the appetite of said mammal, wherein the appetite of the mammal needs to be decreased.

Initially, applicants submit that the combined teachings of the references do not disclose or suggest administering long-chain n-3 polyunsaturated fatty acids (n-3 LC-PUFAs) to any and all obese or overweight individuals. For instance, as discussed above, Phinney, et al. are concerned with providing formulations and methods for the treatment and/or amelioration of symptoms of inflammatory conditions and associated systemic inflammatory responses. Specifically, Phinney, et al. indicate that their formulations (which may comprise n-3 LC-PUFAs) may be useful in countering the symptoms and effects of inflammatory conditions characterized by an elevation of certain biomarkers, such as C-

reactive protein (CRP),[1] and in the reduction of biomarkers associated with inflammation.[2] As recognized by Visser, et al., some overweight or obese individuals may have elevated levels of CRP.

Applicants note, however, that not all obese or overweight individuals have elevated levels of CRP. This is also evidenced by Visser, et al. Specifically, as can be seen from the Figure on the bottom of page 2133 of Visser, et al., the Visser, et al. study found that increasing BMI was correlated with an increase in the prevalence of elevated CRP levels in both men and women,[3] but that not all obese or overweight subjects had elevated (or clinically raised) levels of CRP.[4] Thus, taken together, the combined teachings of Phinney, et al. and Visser, et al. at best suggest administering formulations comprising n-3 LC-PUFAs to individuals having elevated levels of CRP, but do not suggest administering n-3 LC-PUFAs to all obese or overweight individuals, since not all obese or overweight individuals have elevated levels of CRP.

Further, as discussed above, claim 1 requires the appetite of the mammal be one which needs to be decreased. However, not all obese or overweight individuals have an appetite that needs to be decreased. The Office has in fact agreed with this, stating on page 8 of the current action that "it may very well

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[1] Phinney, et al. at p. 5, lines 4-7.
[2] *Id.* at p. 31, lines 32-36.
[3] *See also* Visser, et al. at p. 2132 last paragraph continuing to p. 2133.
[4] Visser, et al. define "overweight" as individuals having a BMI of 25-29.9 kg/m^2, and "obese" as individuals having a BMI of $\geq$ 30 kg/m^2 (*id.* at p. 2132, col. 1, first full paragraph), and define "elevated CRP level" and

be agreed that not *all* obese or overweight mammals have an appetite that needs to be decreased (e.g., such as a patient with a genetic abnormality that causes the obesity and not due simply to overeating)." Thus, the Office is in agreement that not all obese or overweight mammals have an appetite that needs to be decreased. The Office has, however, indicated that even though not all obese or overweight mammals have an appetite that needs to be decreased, Bren provides evidence that of all obese and/or overweight mammals, there is a subpopulation therein that is in need of a reduction in appetite to control the obese and/or overweight condition.

The Office appears to be taking the position that overweight or obese mammals in need of a decrease in appetite is a subgenus of the larger genus of obese or overweight mammals, or more generally, mammals exhibiting elevated levels of C-reactive protein, and that since Phinney, et al. use the formulations described therein for treating patients exhibiting elevated levels of C-reactive protein, this is tantamount to a teaching of the use of the formulations in any subpopulation of patients with elevated C-reactive protein.

Applicants note, however, that MPEP §2144.08, which deals with the obviousness of a species when the prior art teaches a genus, states: "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness." Rather, the patentability of a claim to a specific compound or subgenus

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"clinically raised CRP level" as ≥ 0.22 mg/dL or >1.00 mg/dL, respectively (*id.* at col. 2, last paragraph continuing to top of col. 3).

embraced by a prior art genus should be analyzed no differently than any other claim for purposes of 35 USC 103.

In the instant case, there is nothing in any of the cited references (alone, or in combination) to teach or suggest that administering the formulation of Phinney, et al. will affect the appetite of obese or overweight mammals whose appetite needs to be decreased. Nor is there any suggestion in any of the cited references that decreasing levels of CRP would affect the appetite of an obese or overweight mammal.

In summary, the combined teachings of the cited references do not disclose or suggest administering the formulation of Phinney, et al. to any and all obese or overweight individuals; do not suggest administering the formulation of Phinney, et al. to obese or overweight individuals whose appetite needs to be decreased; and do not suggest any correlation between levels of CRP and appetite in obese or overweight individuals. Thus, applicants submit that one skilled in the art would not be motivated to modify the method of Phinney, et al. to administer the formulations described therein at a time prior to or in conjunction with an appetite-impacting stimulus to decrease appetite of an obese or overweight mammal whose appetite needs to be decreased, as required in the method of applicants' claim 1.

For at least these reasons, and also for the reasons set forth in the response of January 19, 2010, incorporated herein by reference, applicants submit that there is no apparent reason to combine or modify the teachings of the cited references to

arrive at each and every limitation of applicants' claim 1. As such, claim 1 cannot be said to be obvious in view of the cited references.

As claims 2-4, 6, and 30-32 depend directly or indirectly from claim 1, claims 2-4, 6, and 30-32 are patentable for the same reasons as claim 1.

Claim 33 is similar to claim 1, except does not require the limitation that the long-chain n-3 polyunsaturated fatty acid is administered to the mammal for the purpose of decreasing the appetite of the mammal. Claim 33 is thus patentable over the cited references for similar reasons as set forth above for claim 1.

2. Rejection of the Claims under 35 U.S.C. §103(a) over Phinney, et al., Visser, et al., Bogentoft, The Merck Index, and Bren

Reconsideration is requested of the rejection of claims 7-9, 11, and 34 under 35 U.S.C. §103(a) as being unpatentable over Phinney, et al. in view of Visser, et al., Bogentoft (WO 87/03198) in further view of The Merck Index (Monograph 972, page 121), and Bren.

Initially, applicants note that the rejections over Phinney, et al., Visser, et al., Bogentoft, The Merck Index, and Bren are substantially the same as those set forth in the previous Office action dated October 15, 2009. Consequently, many of the Office's comments have previously been addressed in applicants' response of January 19, 2010. For the sake of

brevity, applicants do not now repeat those comments in full, but rather incorporate herein by reference the comments made in the January 19, 2010 response.

Claim 7 is directed to a method for decreasing the appetite of an overweight or obese mammal comprising enterally administering at a time prior to or in conjunction with an appetite-impacting stimulus to the mammal an amount of long-chain n-3 polyunsaturated fatty acid and an amount of long-chain n-6 polyunsaturated fatty acid in amounts effective to decrease the appetite of said mammal, wherein the polyunsaturated fatty acids independently have 20 or more carbon atoms, and wherein the polyunsaturated fatty acids are administered in the form of a triacylglycerol to treat obesity or overweight in mammals that are obese or overweight, and wherein the appetite of the mammal needs to be decreased and the long-chain n-3 polyunsaturated fatty acid and the long-chain n-6 polyunsaturated fatty acid are administered to the mammal for the purpose of decreasing the appetite of the mammal.

Phinney, et al., Visser, et al., and Bren are discussed above.

Bogentoft discloses enteric preparations in the forms of capsules, tablets, and microcapsules having an enteric coating resistant to gastric juices that dissolves only in the ileum. These enteric preparations contain a hydrophobic substance in combination with an emulsifier. The hydrophobic substance is thus delivered to the ileum, at which point it interacts with

specific ileum receptors to induce satiety.[5] The enteric preparation is orally administered in a weight reducing dosage to a human. The hydrophobic substance can be a fatty acid having 6-28 carbon atoms, an ester or a salt thereof, a fatty alcohol having 6-28 carbon atoms or an ester thereof.

The Merck Index discloses the formula and properties for arachidonic acid (AA). Specifically, The Merck Index discloses that AA can occur in depot fats of animals.

For the reasons discussed above, the combined teachings of Phinney, et al., Visser, et al., and Bren do not disclose or suggest administering the formulation of Phinney, et al. (which may comprise an n-3 LC-PUFA) to any and all obese or overweight individuals; do not suggest administering the formulation of Phinney, et al. to obese or overweight individuals whose appetite needs to be decreased; and do not suggest any correlation between levels of CRP and appetite in obese or overweight individuals. Thus, one skilled in the art would not be motivated to modify the method of Phinney, et al. to administer the formulations described therein at a time prior to or in conjunction with an appetite-impacting stimulus to decrease appetite of an obese or overweight mammal whose appetite needs to be decreased, as required in the method of applicants' claim 1. Bogentoft and the Merck Index fail to overcome these shortcomings.

As further discussed in the Amendment and Response After RCE submitted August 21, 2008, while Bogentoft state that its

[5] Bogentoft at p. 2, paragraph 3.

hydrophobic substance can be a fatty acid having 6-28 carbon atoms, Bogentoft actually only disclose and enable fatty acids having up to 18 carbon atoms. The fatty acid can be saturated or unsaturated, and have a branched or a straight chain. The fatty acids include lauric acid, palmitic acid, stearic acid, oleic acid, ricinoleic acid, linoleic acid, and linolenic acid. Accordingly, Bogentoft fails to disclose administering an amount of long chain n-3 polyunsaturated fatty acid, wherein the long chain n-3 polyunsaturated fatty acid has 20 or more carbon atoms, effective in decreasing the appetite of an obese or overweight mammal. Specifically, as described in the instant specification, and as required in claim 7, "long chain n-3 polyunsaturated fatty acid" refers to fatty acids having 20 or more carbons and having a double bond at the third carbon.[6]

As nowhere is it taught or suggested in Bogentoft to administer a long chain n-3 polyunsaturated fatty acid having 20 or more carbon atoms as its hydrophobic substance to be used in the enteric preparation administered for weight loss, applicants respectfully assert that there is simply no apparent reason, based on the combined teachings of the cited references, to administer long-chain n-3 polyunsaturated fatty acid having 20 or more carbon atoms to an obese or overweight mammal at a time prior to or in conjunction with an appetite-impacting stimulus to decrease the appetite of the mammal, wherein the appetite of the mammal needs to be decreased.

[6] *See* Specification at page 16, line 29 through page 17, line 7.

For at least these reasons, and also for the reasons set forth in the response of January 19, 2010, incorporated herein by reference, applicants submit that there is no apparent reason for one skilled in the art to modify or combine the cited references to arrive at the method of claim 7 and, as such, claim 7 is patentable over the combination of Phinney, et al., Visser, et al, Bren, Bogentoft, and The Merck Index.

Claims 8-9 and 11 depend directly or indirectly from claim 7. As such, claims 8-9 and 11 are patentable over the cited references for the same reasons as claim 7 set forth above, as well as for the additional elements they require.

Claim 34 is similar to claim 7, except does not require the limitation that the long-chain n-3 polyunsaturated fatty acid and the long-chain n-6 polyunsaturated fatty acid are administered to the mammal for the purpose of decreasing the appetite of the mammal. As such, claim 34 is patentable over the cited references for similar reasons as set forth above for claim 7.

CONCLUSION

In light of the foregoing, applicants request withdrawal of the rejections of claims 1-11 and 30-34 and allowance of all pending claims. The Commissioner is hereby authorized to charge the fee for a three-month extension of time, as well as any additional government fees which may be required to Deposit Account No. 01-0025.

Respectfully Submitted,

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